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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/788,131	02/16/2001	Adrian Gilbert	60623-A/JPW/GJG/CSN	5640

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EXAMINER	
VANDERVEGT, FRANCOIS P	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 03/24/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/788,131	GILBERT ET AL.	
	Examiner	Art Unit	
	F. Pierre VanderVegt	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE ____ MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-35,37-43,50-55 and 61-74* is/are pending in the application.

4a) Of the above claim(s) *55 and 67-74* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-35,37-43,50-54 and 61-66* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12182003*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This application claims the benefit of the filing date of Provisional Application No. 60/183,666, filed February 18, 2000.

Claims 2, 36, 44-49 and 56-60 have been canceled.

Claims 67-74 have been newly added.

Claims 1, 3-35, 37-43, 50-55 and 61-74 are currently pending.

Election/Restrictions

1. In the amendment filed November 3, 2003 Applicant has continued to traverse the withdrawal of claim 55 by the Examiner, asserting that the claim was improperly withdrawn because elected claim 50, drawn to a product, constitutes a linking claim that links the method of making the product in claim 43 with the method of using the product in claim 55. Applicant argues that a similar argument can be applied to new method of use claims 67-74.

Applicant's arguments are not convincing for the reasons made of record in the restrictiction requirement mailed April 22, 2002, namely, because the product of Group I (including claim 50) has a separate utility than that of the method of Group II (including claim 55).

Applicant is invited to note, however, that when applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is

advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.**

Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Accordingly, **claims 55 and 67-74 are withdrawn.**

Claims 1, 3-35, 37-43, 50-54 and 61-66 are the subject of examination in the present Office Action.

2. In view of Applicant's amendment filed November 3, 2003 and the evidence of common ownership of the instant application and U.S. Patent No. 6,214,791 to Arnon et al, only the following grounds of rejection are maintained.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

3. Claims 1, 3-35, 37-43, 50-54 and 62, 63 and 65 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 7-14 of U.S. Patent No. 6,214,791 to Arnon et al (on form PTO-1449 filed July 8, 2002 – courtesy copy filed May 5, 2003) in view of U.S. Patent No. 6,024,981 to Khankari et al (A on form PTO-892)

It was previously stated: "Specifically, claims 7-11 of the '791 patent are drawn to the use of copolymer-1 for the manufacture of a medicament or pharmaceutical composition for the treatment of multiple sclerosis via ingestion or inhalation (7), wherein the medicament comprises 0.1-1000 mg of

copolymer-1 (8), is formulated for oral or nasal administration (9), is administered via inhalation (10), or is enterically coated (11). Claim 7 of the '791 patent is a genus claim which broadly encompasses the presently claimed method of making a copolymer-1 medicament in light of the disclosure of the '981 patent [Instant claims 43 and 64-65]. Claims 12-14 are drawn to a pharmaceutical composition for the treatment of multiple sclerosis via ingestion or inhalation (12), wherein the pharmaceutical composition is in solid, liquid, aerosol or inhalable powder form (13), or is enterically coated (14). Claim 12 of the '791 patent is a genus claim which broadly encompasses the presently claimed pharmaceutical composition in light of the further disclosure of the '791 patent and the disclosure of the '981 patent.

The pharmaceutical composition recited in claim 12 of the '791 patent comprises as an active ingredient a therapeutically effective amount of Copolymer 1(glatimer acetate). As is evidenced by the disclosure of the '791 patent, the composition is used to treat multiple sclerosis by oral administration of copolymer-1 through ingestion, and that when copolymer-1 is introduced orally it may be in solid form, and it may be mixed with pharmaceutically acceptable carrier. The disclosure of the '791 patent indicates that the use of enteric coatings is well known in the art, including methacrylic acid copolymer (Eudragit L; column 3, lines 27-42 in particular)[Instant claims 18, 20, 29-31]. The '791 patent further discloses that the administration of the composition orally, nasally or bronchially in liquid or solid form with a range of copolymer-1 from 0.1 to 1000 mg (column 2, line 45 to column 3, line 26) [claims 23-28, 32-42, 50-54, 62-63].

The '791 patent does not specifically recite that said carrier is microcrystalline cellulose or admixture with a lubricant.

Microcrystalline cellulose is well known in the art as a stable and physiologically inert exipient. The '981 patent teaches that microcrystalline cellulose is a non-effervescent wicking or disintegration agent for solid compositions such as tablets (column 13, lines 47-59 in particular) and that tablets can be made in unit dosage forms adapted for oral administration (column 4, lines 30-35). The '981 patent teaches that the percentage of active ingredient, and therefore of the carrier in proportion to that active ingredient, in a solid pharmaceutical preparation may be selected according to known principals of pharmacy (column 5, lines 12-14 in particular). The '981 patent teaches that the active ingredient used can vary greatly and is generally provided in an amount between greater than zero and 80% (column 5, lines 34-56 in particular). The '981 patent teaches that a typical range for a disintegrant such as microcrystalline cellulose is conventionally as high as 20% but can be increased for rapidly disintegrating dosage forms (column 13, lines 60-67 in particular)[Instant claims 1, 3-8]. The '981 patent also teaches modified starches as a disintegration agent (column 13, lines 47-59 in particular)[Claims 8-14]. The '981 patent further teaches lubricants, including magnesium stearate (column 10, lines 13-51 in particular)[claims 15-17]. Claims 34-35 are included because the use of preservatives in pharmaceutical formulations is well known to enhance the longevity of the formulation in storage.

Accordingly, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to manufacture a composition comprising copolymer-1 as recited in claims 7-14 of the '791 patent using the well-known microcrystalline cellulose as an exipient and magnesium stearate as a lubricant, optimizing the proportions of active ingredient as taught by the '981 patent. One would have been motivated to combine these teachings because thus formed composition can be used as a medicament."

Applicant's arguments filed November 3, 2003 have been fully considered but they are not persuasive. Applicant asserts that the instant invention is novel and unobvious over the cited references because none of the references specifically teach the combination of glatiramer acetate (copolymer-1) as an active ingredient with microcrystalline cellulose (MCC) as a carrier. Applicant further asserts that

none of the references teach the use of at least 50% MCC in the formulation of a medicament. As stated previously, MCC is well known in the art as a stable and physiologically inert exipient. Applicant argues that the '981 patent teaches away from the use of such high proportions of MCC in a medicament because none of the specific examples of the '981 patent uses that much. However, the '981 patent does teach that a typical range for a disintegrant such as microcrystalline cellulose is conventionally as high as 20% but can be increased for rapidly disintegrating dosage forms (column 13, lines 60-67 in particular). The fact that that there are no specific examples with such a high proportion does not negate the fact that high percentages of disintegrant is taught by the '981 patent when rapid disintegration is desired. Applicant's use of greater than 50% MCC in the formulation of a medicament comprising glatiramer acetate represents optimization of a formulation for enhanced dissolution properties and this is a skill that is well within the purview of a person having ordinary skill in the art at the time the invention was made and does not require particular inventive input. Contrary to Applicant's assertion that the '981 patent teaches away from 50% MCC in the medicament, based upon the cited teachings of the '981 patent the artisan would have a reasonable expectation of success in improving the rapid dissolution of the medicament by the use of percentages of MCC higher than 20% and a reasonable expectation of success is all that is required by the statute (*In re* Vaeck, 20 USPQ 1438 (Fed. Cir. 1991)).

4. Claims 1, 20, 21, 22, 43 and 64 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 7-14 of U.S. Patent No. 6,214,791 to Arnon et al (on form PTO-1449 filed July 8, 2002 – courtesy copy filed May 5, 2003) in view of U.S. Patent No. 6,024,981 to Khankari et al (A on form PTO-892) and U.S. Patent No. 5,965,600 to Sato et al (B on form PTO-892).

It was previously stated: "The '791 and '981 patents have been discussed supra.

The combined disclosures do not specifically recite film coating of the solid form in combination with the enteric coating.

The '600 patent teaches a medicament in tablet form comprising both an enteric coating and a film coating, which could be polyvinyl alcohol (column 4, lines 39-62 in particular).

It would have been prima facie obvious to a person having ordinary skill in the art at the time the invention was made to combine the teachings of the '600 patent with the combined disclosures of the '791 and '981 patents. One would have been motivated to combine the references with a reasonable expectation of success by the teaching of the '600 patent that multiple coatings of a tablet including both enteric and film coatings is "customary" in the art."

Applicant argues that the citation of the '600 patent does not render the combination of glatiramer acetate (copolymer-1), greater than 50% MCC and an enteric coating obvious. The combination of glatiramer acetate and MCC has been discussed supra. in section 3. Contrary to Applicant's assertion, the

use of an enteric coating on the claimed medicament would have been obvious to the artisan because the use of both enteric and film coatings is "customary" in the art and in the present instance would be particularly so because, as a proteinaceous active ingredient, glatiramer acetate would be particularly subject to acidic degradation in the stomach, which may reduce it's effectiveness in the treatment of MS.

5. Claims 1 and 61 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 12-14 of U.S. Patent No. 6,214,791 to Arnon et al (on form PTO-1449 filed July 8, 2002 – courtesy copy filed May 5, 2003) in view of U.S. Patent No. 6,024,981 to Khankari et al (A on form PTO-892) and U.S. Patent No. 6,162,800 to Dolle et al (C on form PTO-892).

It was previously stated: "The '791 and '981 patents have been discussed supra.
The combined disclosures do not specifically recite protease inhibitors in a medicament for multiple sclerosis.
The '800 patent teaches a pharmaceutical composition comprising a protease inhibitor for the treatment of IL-1β mediated disease states (column 7, lines 39-56 in particular).
It would have been prima facie obvious to a person having ordinary skill in the art at the time the invention was made to combine the teachings of the '800 patent with the combined disclosures of the '791 and '981 patents. One would have been motivated to combine the references with a reasonable expectation of success by the teaching of the '800 patent that multiple sclerosis is an IL-1β mediated disease state which can be treated with medicaments comprising a protease inhibitor."

Applicant argues that the citation of the '800 patent does not render the combination of glatiramer acetate (copolymer-1), greater than 50% MCC and a protease inhibitor obvious. The combination of glatiramer acetate and MCC has been discussed supra. in section 3. Contrary to Applicant's assertion, the use of a protease inhibitor as part of the claimed medicament would have been obvious to the artisan because the '800 patent specifically teaches the benefit of the inclusion of a protease inhibitor as an element of a pharmaceutical composition for the treatment of IL-1β mediated disease states, including MS.

6. Claims 43, 65 and 66 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 7-11 of U.S. Patent No. 6,214,791 to Arnon et al (on form PTO-1449 filed July 8, 2002 – courtesy copy filed May 5, 2003) in view of U.S. Patent No. 6,024,981 to Khankari et al (A on form PTO-892) and U.S. Patent No. 4,129,666 to Wizerkaniuk (D on form PTO-892).

It was previously stated: "The '791 and '981 patents have been discussed supra.
The combined disclosures do not specifically recite the use of a rotating pan for application of the enteric coating to the solid form of the pharmaceutical composition.

The '666 patent teaches the application of enteric coating medicinal pellets with an enteric coating using a rotating pan apparatus (entire patent).

It would have been prima facie obvious to a person having ordinary skill in the art at the time the invention was made to combine the teachings of the '666 patent with the combined disclosures of the '791 and '981 patents. One would have been motivated to combine the references with a reasonable expectation of success by the teaching of the '666 patent that methods of applying an enteric coating such as spraying requires the use of solvents which may be toxic, while the rotating pan method does not require such solvents (column 1, lines 24-56 in particular)."

Applicant argues that the citation of the '666 patent does not render the combination of glatiramer acetate (copolymer-1), greater than 50% MCC and the use of a rotating pan apparatus for the application of an enteric coating obvious. The combination of glatiramer acetate and MCC has been discussed supra. in section 3. Contrary to Applicant's assertion, the use of a rotating pan apparatus for the application of an enteric coating to the claimed medicament would have been obvious to the artisan because the use of such an apparatus does not require the use of toxic solvents, thus being beneficial both for the recipient subject and for workers of the manufacturing facility.

Conclusion

7. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to F. Pierre VanderVegt whose telephone number is (571) 272-0852. The examiner can normally be reached on M-Th 6:30-4:00; Alternate Fridays 6:30-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

F. Pierre VanderVegt, Ph.D.
Patent Examiner
March 19, 2004

PATRICK J. NOLAN, PH.D.
PRIMARY EXAMINER
3/22/04